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Role of Non HLA Genetic Variants in End Stage Renal Disease

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Cytokines and intercellular adhesive molecules (ICAM) play a crucial role in the pathogenesis of primary kidney disease and progression to end stage renal disease (ESRD). Cytokine secretion is reported to be dependent upon the SNP's located in the cytokine genes. The role of different polymorphisms of cytokines and ICAM genes as a probable susceptibility factors for ESRD have been explored in the present study.

The study was conducted on 258 ESRD patients and ethnically matched 569 controls. Individuals were genotyped for *IL-6* (G174C), *IL-4* (C590T), *TNF-α* (-G308A and -G238A) and *ICAM-1* (A469G) gene polymorphisms using standard PCR-RFLP based method.

We observed significant difference in the genotype frequencies of the *TNF-α* -308AA (p=0.001, OR=7.61, 95%CI=2.1-27.9), *TNF-α* -238AA (p=0.001, OR=5.8, 95%CI=2.2–15.1). Further, C allele of *IL-6* -G174C and G allele of *ICAM-1* A469G were significantly different in ESRD patients when compared to controls (p=0.0001; OR=5.5, 95%CI=3.9-7.7 and p<0.0001; OR=3.8, 95%CI=3.1-4.7). For the *IL-4* C590T polymorphism, though the homozygous mutant genotype (TT) was not found to be significantly associated with ESRD, a statistically significant association with T allele (p=0.0001) was found with the ESRD. Further, combined analysis revealed a higher risk in ESRD patients with low *IL-4* and high *IL-6* producing genotypes and high producing genotype of *TNF-α* (308 and 238) with the increased risk of ~6.0 fold and 3.3 fold respectively. Our results suggest that *IL-6, IL-4, TNF-α* and *ICAM* gene polymorphism may be risk factors for ESRD.